

## \* NOTICES \*

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## DETAILED DESCRIPTION

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[Detailed Description of the Invention]

[0001]

[Industrial Application]This invention relates to the anti-Helicobacter Pylori medicine containing the extract of the dry root of MORINDA SHITORIFORIA.

[0002]

[Description of the Prior Art]The validity of the Helicobacter Pylori (Helicobacter pylori) disinfection therapy in a peptic ulcer therapy is checked by both sides of early recovery of an ulcer, and recurrence prevention, 3 agent combined therapy (two sorts of antibiotics, and bismuth preparation) (for example, JI American journal gastroenterology [ the Am.J. ] [of Gastroenterology] 87-volume 1716 page 1992), The combined therapy (for example, JI American journal gastroenterology [ the Am.J. ] [of Gastroenterology] 88-volume 491 page 1993) of a protonpump inhibitor and an antibiotic is known. In the Helicobacter Pylori disinfection therapy in a peptic ulcer therapy, it becomes unnecessary [ the maintenance therapy aiming at recurrence prevention ], and there is an effect of decline in a rate of recurrence, shortening of the time to recovery, and reduction of the costs of medical treatment compared with an H<sub>2</sub> blocker or a defense factor enhancement agent.

[0003]Yne When a living body is medicated, all have [ antibiotics in which an antibacterial action is shown to Helicobacter Pylori by a vitro (inch vitro) ] a low rate of eradication in single \*\*. Therefore, although 2 agent and 3 agent combined therapy (an antibiotic and bismuth preparation), the combined therapy of a protonpump inhibitor and an antibiotic, etc. are examined and the effective thing is already known, all include the problem. For example, I hear that there is possibility of an appearance of needing the numerousness of the frequency of frequency of administration and the extensive administration more than a usual dose, side effects, such as diarrhea and constipation, and resistant bacteria, and it is. Therefore, in such a case, for the purpose of the Helicobacter Pylori disinfection in a peptic ulcer therapy, it is

alternative to Helicobacter Pylori and the high drug of the rate of eradication in single \*\* is needed.

[0004]

[Problem(s) to be Solved by the Invention]An object of this invention is to provide the useful anti-Helicobacter Pylori medicine for disinfection of Helicobacter Pylori in the therapy of the top digestive system disease resulting from Helicobacter pylori infection.

[0005]

[Means for solving problem]The result of having examined wholeheartedly the substance in which this invention persons have the Helicobacter Pylori disinfection operation in a peptic ulcer therapy, It finds out that specific vegetation and MORINDA SHITORIFORIA (Morinda citrifolia: Japanese-name Indian mulberry) (Dicotyledoneae, Rubiaceae) have the Helicobacter Pylori disinfection operation, and came to complete this invention.

[0006]This invention in alignment with the above-mentioned purpose is the anti-Helicobacter Pylori medicine containing the extract of the dry root of MORINDA SHITORIFORIA. This invention is the useful anti-Helicobacter Pylori medicine for disinfection of Helicobacter Pylori in the therapy of the top digestive system disease resulting from Helicobacter pylori infection, and this invention can serve as a recurrence preventive medicine of a more effective peptic ulcer. It is effective as the remedy or preventive medicine of various symptoms in which Helicobacter Pylori participates.

[0007]The anti-Helicobacter Pylori medicine containing the extract of the dry root of MORINDA SHITORIFORIA of this invention can be obtained as follows. The extract of the dry root of MORINDA SHITORIFORIA adds the suitable organic solvent or water for the above-mentioned dry matter, and is obtained a room temperature or by heating and carrying out extracting processing, filtering an extraction mixture, and carrying out decompression distilling off of the solvent from filtrate. As an example of the organic solvent used as an extracting solvent, alcohol like methanol, ethanol, n-propanol, isopropanol, and n-butanol, pyridine, hexane, ethyl acetate, acetone, chloroform, a methylene chloride, etc. are mentioned. In particular, methanol and chloroform are preferred. Although it decides on extracting processing time suitably according to the kind of raw material, quality, etc., it is usually several hours - a two-day grade. It is more desirable to grind the above-mentioned dry matter in advance of extracting processing operation of the above-mentioned dry matter of this invention.

[0008]The anti-Helicobacter Pylori medicine containing the extract of the dry root of MORINDA SHITORIFORIA of this invention can be used as preventive effective in the disease resulting from Helicobacter Pylori, and a treating agent, For example, although it is used as a peptic ulcer, gastritis and a hepatitis remedy, and recurrence preventive of a peptic ulcer, gastritis, hepatitis, gastric cancer, and hepatic carcinoma and a dose changes with condition, Generally, it is 1-1000 mg preferably, and it is [ adult daily dose of 0.10-3000 mg ] good to prescribe a

medicine for the patient in 1 to 4 steps as occasion demands according to condition. It can take arbitrary forms suitable for administration, and although especially the internal use of a medication method is desirable, it can also be injected intravenously.

[0009]The anti-Helicobacter Pylori medicine of this invention can take the arbitrary formulation which was independent or was suitable for administration of a tablet, powder medicine, a capsule, a granule, syrups, liquor, suspension, injections, ophthalmic solutions, or a suppository by publicly known pharmaceutical preparation technology with the pharmaceutical preparation carrier as one of the active principles. As a concrete pharmaceutical preparation carrier, starch, sucrose, milk sugar, methyl cellulose, Carboxymethyl cellulose, crystalline cellulose, sodium alginate, Calcium hydrogen phosphate, magnesium aluminometasilicate, a silicic acid anhydride, And excipients, such as synthetic aluminum silicate, hydroxypropylcellulose, Binding materials, such as hydroxypropylmethylcellulose, gelatin, and a polyvinyl pyrrolidone, Disintegration agents, such as carboxymethyl-cellulose calcium, bridge construction carboxymethylcellulose sodium, and a bridge construction polyvinyl pyrrolidone, Lubricant, such as magnesium stearate and talc, cellulose acetate phthalate, Coating, such as hydroxypropylmethylcellulose acetate succinate, methacrylic acid, and methyl methacrylate copolymer, Solubilizing agents, such as a polyethylene glycol, sodium lauryl sulfate, Chelating agents, such as emulsifiers, such as lecithin, sorbitan monooleate, polyoxyethylene cetyl ether, sucrose fatty acid ester, polyoxyethylene hydrogenated castor oil, and glyceryl monostearate, and EDTA, a buffer, a moisturizer, an antiseptic, cacao oil -- and -- oui, the base of TEBUZORU W35 grade can be mentioned.

[0010]

[Working example]Next, an embodiment and the example of an examination are shown and this invention is explained still more concretely.

[0011](Embodiment 1) 200 g of dry roots of MORINDA SHITORIFORIA are ground, It agitated with 2.0 l. of chloroform for 2 hours, and this was filtered, the same operation was repeated again, it agitated further 2.0 l. of chloroform, and overnight, decompression distilling off of the organic layer which filtered and united this was carried out, and 2.40 g of chloroform crude extracts were obtained.

[0012](Example 1 of an examination) The anti-Helicobacter Pylori operation of the anti-Helicobacter Pylori medicine which contains the extract of the dry root of MORINDA SHITORIFORIA of this invention by measurement of the in vitro anti-Helicobacter Pylori operation minimum inhibitory concentration (Media Interface Connector) was measured.

[0013]The Helicobacter Pylori barometer stock (NCTC 11916) and clinical isolate are inoculated into a horse defibrinated blood addition SUKIRO agar plate 5%, and preculture is carried out for three to five days at a microaerophilic condition (10%CO<sub>2</sub>, 5%O<sub>2</sub>, 85%N<sub>2</sub>) and 37 \*\*. The extract of the dry root of MORINDA SHITORIFORIA obtained in Embodiment 1 is

dissolved in dimethyl sulfoxide (dimethylsulfoxide:DMSO), Two steps are diluted and it adds to a horse defibrinated blood addition SUKIRO agar plate 5% so that it may become 1-400 microg (1% or less of dimethyl sulfoxide final concentration)/ml final concentration, and the agar plate for Media Interface Connector measurement is created. It extracts from the agar plate which carried out preculture of the Helicobacter Pylori barometer stock and the clinical isolate, and suspends to a physiological salt solution, and  $10^8$ CFU/ml fungus liquid is obtained. This fungus liquid is inoculated into the agar plate surface for Media Interface Connector measurement in a cross-joint streak, and it cultivates for one week at a microaerophilic condition ( $10\%CO_2$ ,  $5\%O_2$ ,  $85\%N_2$ ) and  $37^\circ C$ . The agar plate with which the agar plate for Media Interface Connector measurement is observed, and the cross joint is permitted growth of Helicobacter Pylori on the agar plate surface, Divide the agar plate which is not accepted and the agar plate of the minimum density which shows continuity to the addition of the extract of the dry root of MORINDA SHITORIFORIA of this invention among the agar plates with which growth is not accepted is found out, Let the addition be a minimum inhibitory concentration (Media Interface Connector) to this Helicobacter pylori stock of the extract of the dry root of MORINDA SHITORIFORIA of this invention.

[0014]As a result, Media Interface Connector of the extract of the dry root of MORINDA SHITORIFORIA of this invention is 6.25 microg/ml, and showed the outstanding anti-Helicobacter Pylori operation.

[0015](Acute toxicity) The acute toxicity test by internal use was done using the ICR system male mouse (five weeks old). Each  $LD_{50}$  value of the extract of the dry root of MORINDA SHITORIFORIA of this invention is 1000 or more mg/kg, and high safety was confirmed.

[0016]

[Effect of the Invention]Since the anti-Helicobacter Pylori medicine containing the extract of the dry root of MORINDA SHITORIFORIA of this invention has the anti-Helicobacter Pylori operation as shown in the example of an examination, it is effective as the preventive and the remedy of the top digestive system disease resulting from Helicobacter Pylori. It is especially effective as a peptic ulcer, gastritis and a hepatitis remedy, and recurrence preventive of a peptic ulcer, gastritis, hepatitis, gastric cancer, and hepatic carcinoma.

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[Translation done.]